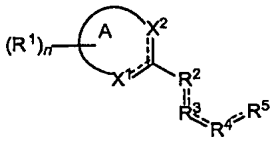
CLAIMS

What is claimed is:

1. A method of treating a neoplastic disease or a proliferative disorder in a human comprising administering a therapeutically effective amount of a compound having the formula I



(I)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^2 is selected from $-CR^{21}{}_a-$, $-NR^{22}{}_b-$, and $-(C=R^{23})-$;

each R^{21} is independently selected from H, halo, $-NH_2$, $-N(H)(C_{1-3}$ alkyl), $-N(C_{1-3}$ alkyl$)_2$, $-O-(C_{1-3}$ alkyl), OH and C_{1-3} alkyl;

each R^{22} is independently selected from H and C_{1-3} alkyl;

R^{23} is selected from O, S, N-R^0, and N-OR^0;

R^3 is selected from $-CR^{31}_{c}-$, $-NR^{32}_{d}-$, and -(C=R^{33})-;

each R^{31} group is selected from H, halo, $-NH_2$, -N(H)(R^0), -N(R^0)$_2$, -O-R^0, OH and C_{1-3} alkyl;

each R^{32} group is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, C(O)R^0, aryl, and a heterocyclic ring;

R^{33} is selected from O, S, N-R^{34}, and N-OR^0;

R^{34} is selected from H, NO_2, CN, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl and a heterocyclic ring;

R^4 is selected from $-CR^{41}_{e}-$, $-NR^{42}_{f}-$, -(C=R^{43})-, and -O-;

each R^{41} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, CO_2R^0, C(O)R^0, aralkyl, aryl, and a heterocyclic ring;

each R^{42} group is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, C(O)R^0, aryl, and a heterocyclic ring;

each R^{43} is selected from O, S, N-R^0, and N-OR^0;

with the provisos that when R^2 is $-NR^{22}_{b}-$ and R^4 is $-NR^{42}_{f}-$, then R^3 is not $-NR^{32}_{d}-$; and that both R^3 and R^4 are not simultaneously selected from -(C=R^{33})- and -(C=R^{43})-, respectively;

R^5 is selected from -Y-R^6 and -Z-R^7;

Y is selected from a chemical bond, O, NR^0,

R^6 is selected from alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

Z is a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, C(O)R^0, C(O)N(R^0)$_2$, CN, CF_3, N(R^0)$_2$, NO_2, and OR^0;

R^7 is H or is selected from aryl and a heterocyclic ring;

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring;

a is 1 or 2;

b is 0 or 1;

c is 1 or 2;

d is 0 or 1;

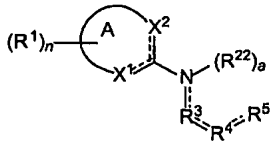
e is 1 or 2; and

f is 0 or 1.

2. The method of claim 1 wherein X^1 is N.

3. The method of claim 2 wherein X^2 is N.

4. The method of claim 1, comprising administering a therapeutically effective amount of a compound having the formula I_a



(I_a)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

each R^{22} is independently selected from H and C_{1-3} alkyl;

R^3 is selected from $-CR^{31}{}_c-$, $-NR^{32}{}_d-$, and $-(C=R^{33})-$;

each R^{31} group is selected from H, halo, $-NH_2$, $-N(H)(R^0)$, $-N(R^0)_2$, $-O-R^0$, OH and C_{1-3} alkyl;

each R^{32} group is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, aryl, and a heterocyclic ring;

R^{33} is selected from O, S, $N-R^{34}$, and $N-OR^0$;

R^{34} is selected from H, NO_2, CN, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl and a heterocyclic ring;

R^4 is selected from $-CR^{41}{}_{e}-$, $-NR^{42}{}_{f}-$, $-(C=R^{43})-$, and -O-;

each R^{41} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, CO_2R^0, $C(O)R^0$, aralkyl, aryl, and a heterocyclic ring;

each R^{42} group is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, aryl, and a heterocyclic ring;

each R^{43} is selected from O, S, $N-R^0$, and $N-OR^0$;

with the provisos that when R^4 is $-NR^{42}{}_{f}-$, then R^3 is not $-NR^{32}{}_{d}-$; and that both R^3 and R^4 are not simultaneously selected from $-(C=R^{33})-$ and $-(C=R^{43})-$, respectively;

R^5 is selected from $-Y-R^6$ and $-Z-R^7$;

Y is selected from a chemical bond, O, $N-R^0$,

R^6 is selected from alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

Z is a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

R^7 is H or is selected from aryl and a heterocyclic ring;

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring;

a is 1 or 2;

b is 0 or 1;

c is 1 or 2;

d is 0 or 1;

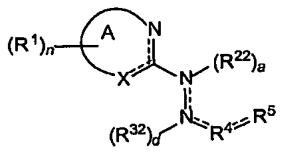
e is 1 or 2; and

f is 0 or 1.

5. The method of claim 4 wherein X^1 is N.

6. The method of claim 5 wherein X^2 is N.

7. The method of claim 1, comprising administering a therapeutically effective amount of a compound having the formula I_b



(I_b)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

each R^{22} is independently selected from H and C_{1-3} alkyl;

each R^{32} group is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, aryl, and a heterocyclic ring;

R^4 is selected from $-CR^{41}{}_e-$, $-(C=R^{43})-$, and -O-;

each R^{41} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, CO_2R^0, $C(O)R^0$, aralkyl, aryl, and a heterocyclic ring;

each R^{43} is selected from O, S, N-R^0, and N-OR^0;

R^5 is selected from -Y-R^6 and -Z-R^7;

Y is selected from a chemical bond, O, N-R^0,

R^6 is selected from alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

Z is a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

R^7 is H or is selected from aryl and a heterocyclic ring;

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring;

a is 1 or 2;

b is 0 or 1;

c is 1 or 2;

d is 0 or 1;

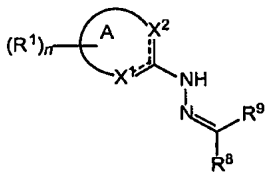
e is 1 or 2; and

f is 0 or 1.

8. The method of claim 7 wherein X^1 is N.

9. The method of claim 8 wherein X^2 is N.

10. The method of claim 1, comprising administering a therapeutically effective amount of a compound having the formula II



(II)

wherein

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^8 is selected from the group consisting of is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, CO_2R^0, $C(O)R^0$, aralkyl, aryl, and a heterocyclic ring;

R^9 is selected from -Y-R^6 and -Z-R^7;

Y is selected from a chemical bond, O, N-R^0,

R^6 is selected from alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

Z is a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

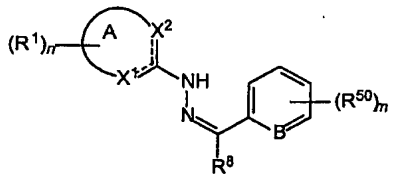
R^7 is H or is selected from aryl and a heterocyclic ring; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

11. The method of claim 10 wherein X^1 is N.

12. The method of claim 11 wherein X^2 is N.

13. The method of claim 1, comprising administering a therapeutically effective amount of a compound having the formula II_a



(II_a)

wherein

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$,$-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^8 is selected from the group consisting of is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, CO_2R^0, $C(O)R^0$, aralkyl, aryl, and a heterocyclic ring;

X^3 is N, CH or C-R^{50};

each R^{50} is independently selected from the group consisting of alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{51}, $-(CH_2)_rC(O)(CH_2)_sR^{51}$, $-(CH_2)_rC(O)N(R^{52})(R^{53})$, $-(CH_2)_rC(O)O(CH_2)_sR^{51}$,$-(CH_2)_rN(R^{51})C(O)R^{51}$, $-(CH_2)_rN(R^{52})(R^{53})$, $-N(R^{51})SO_2R^{51}$,

$-OC(O)N(R^{52})(R^{53})$, $-SO_2N(R^{52})(R^{53})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^{50} groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

R^{51} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

R^{52} and R^{53} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{52} and R^{53} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

r is 0 to 4;

s is 0 to 4;

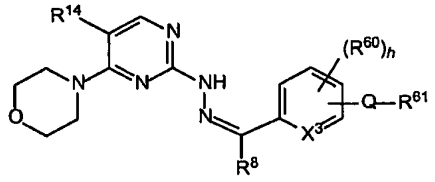
m is 0 to 4; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

14. The method of claim 13 wherein X^1 is N.

15. The method of claim 14 wherein X^2 is N.

16. The method of claim 1, comprising administering a therapeutically effective amount of a compound having the formula II_b



wherein:

R^{14} is selected from H and F;

R^8 is selected from the group consisting of is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, CO_2R^0, $C(O)R^0$, aralkyl, aryl, and a heterocyclic ring;

X^3 is N, CH or C-R^{60};

each R^{60} is independently selected from the group consisting of alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^0, halo, aryl, and a heterocyclic ring;

R^{61} is selected from aryl and a heterocyclic ring;

Q is selected from a chemical bond or a group having the formula -O-, -$(CH_2)_i$-, -$(CH_2)_iC(O)(CH_2)_j$-, -$(CH_2)_i$-$N(R^{62})$-$(CH_2)_j$-, -$(CH_2)_iC(O)$-$N(R^{62})$-$(CH_2)_j$-, -$(CH_2)_iC(O)O(CH_2)_j$-, -$(CH_2)_iN(R^{62})C(O)$-$(CH_2)_j$-, -$(CH_2)_iOC(O)N(R^{62})$-$(CH_2)_j$-, and -O-$(CH_2)_i$-$C(O)N(R^{62})$-$(CH_2)_j$-;

R^{62} is selected from aryl, and a heterocyclic ring;

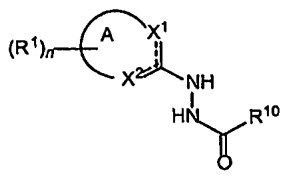
each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring;

h is 0 to 4;

i is 0 to 4; and

j is 0 to 4.

17. The method of claim 1, comprising administering a therapeutically effective amount of a compound having the formula III



(III)

wherein

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, -$(CH_2)_pC(O)(CH_2)_qR^{11}$, -$(CH_2)_pC(O)N(R^{12})(R^{13})$, -$(CH_2)_pC(O)O(CH_2)_qR^{11}$,-$(CH_2)_pN(R^{11})C(O)R^{11}$, -$(CH_2)_pN(R^{12})(R^{13})$, -$N(R^{11})SO_2R^{11}$, -$OC(O)N(R^{12})(R^{13})$, -$SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken

together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^{10} is selected from -Y'-R^{18};

Y' is selected from a chemical bond, O, NR^0-, and a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

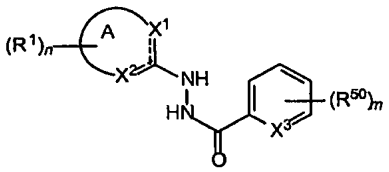
R^{18} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CF_3, aryl, and a heterocyclic ring; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

18. The method of claim 17 wherein X^1 is N.

19. The compound of claim 18 wherein X^2 is N.

20. The method of claim 1, comprising administering a therapeutically effective amount of a compound having the formula III_a



(III_a)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused

ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

X^3 is N, CH or C-R^{50};

each R^{50} is independently selected from the group consisting of alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{51}, $-(CH_2)_rC(O)(CH_2)_sR^{51}$, $-(CH_2)_rC(O)N(R^{52})(R^{53})$, $-(CH_2)_rC(O)O(CH_2)_sR^{51}$, $-(CH_2)_rN(R^{51})C(O)R^{51}$, $-(CH_2)_rN(R^{52})(R^{53})$, $-N(R^{51})SO_2R^{51}$, $-OC(O)N(R^{52})(R^{53})$, $-SO_2N(R^{52})(R^{53})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^{50} groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

R^{51} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

R^{52} and R^{53} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{52} and R^{53} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

r is 0 to 4;

s is 0 to 4;

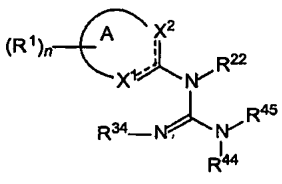
m is 0 to 4; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

21. The method of claim 20 wherein X^1 is N.

22. The method of claim 21 wherein X^2 is N.

23. The method of claim 1, comprising administering a therapeutically effective amount of a compound having the formula IV



(IV)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^{22} is selected from H and C_{1-3} alkyl;

R^{34} is selected from H, NO_2, CN, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl and a heterocyclic ring;

R^{44} is selected from H, alkyl, cycloalkyl, $-(C=O)R^0$, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

R^{45} is selected from -Y"-R^{19};

Y" is selected from a chemical bond, O, NR^0-, and a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

R^{19} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CF_3, aryl, and a heterocyclic ring; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

24. The method of claim 23 wherein X^1 is N.

25. The method of claim 24 wherein X^2 is N.

26. The method of claim 1, comprising administering a therapeutically effective amount of a compound having the formula V

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wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken

together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^{22} is selected from H and C_{1-3} alkyl;

R^{34} is selected from H, NO_2, CN, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl and a heterocyclic ring;

R^{55} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

R^{56} is selected from -Y"-R^{19};

Y" is selected from a chemical bond, O, NR^0-, and a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

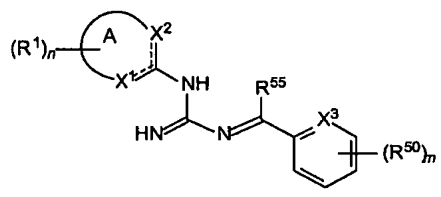
R^{19} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CF_3, aryl, and a heterocyclic ring; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

27. The method of claim 26 wherein X^1 is N.

28. The method of claim 27 wherein X^2 is N.

29. The method of claim 1, comprising administering a therapeutically effective amount of a compound having the formula V_a



(V_a)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^{55} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

X^3 is N or C-R^{50};

each R^{50} is independently selected from the group consisting of alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{51}, $-(CH_2)_rC(O)(CH_2)_sR^{51}$, $-(CH_2)_rC(O)N(R^{52})(R^{53})$, $-(CH_2)_rC(O)O(CH_2)_sR^{51}$, $-(CH_2)_rN(R^{51})C(O)R^{51}$, $-(CH_2)_rN(R^{52})(R^{53})$, $-N(R^{51})SO_2R^{51}$, $-OC(O)N(R^{52})(R^{53})$, $-SO_2N(R^{52})(R^{53})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^{50} groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

R^{51} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

R^{52} and R^{53} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{52} and R^{53} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

r is 0 to 4;

s is 0 to 4;

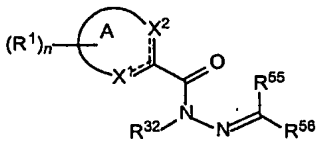
m is 0 to 4; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

30. The method of claim 29 wherein X^1 is N.

31. The method of claim 30 wherein X^2 is N.

32. The method of claim 1, comprising administering a therapeutically effective amount of a compound having the formula VI



(VI)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^{55} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

R^{56} is selected from -Y"-R^{19};

Y" is selected from a chemical bond, O, NR^0-, and a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

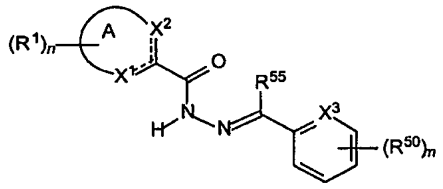
R^{19} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CF_3, aryl, and a heterocyclic ring; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

33. The method of claim 32 wherein X^1 is N.

34. The method of claim 33 wherein X^2 is N.

35. The method of claim 1, comprising administering a therapeutically effective amount of a compound having the formula VI_a



(VI_a)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused

ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^{55} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

X^3 is N or C-R^{50};

each R^{50} is independently selected from the group consisting of alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{51}, $-(CH_2)_rC(O)(CH_2)_sR^{51}$, $-(CH_2)_rC(O)N(R^{52})(R^{53})$, $-(CH_2)_rC(O)O(CH_2)_sR^{51}$, $-(CH_2)_rN(R^{51})C(O)R^{51}$, $-(CH_2)_rN(R^{52})(R^{53})$, $-N(R^{51})SO_2R^{51}$, $-OC(O)N(R^{52})(R^{53})$, $-SO_2N(R^{52})(R^{53})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^{50} groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

R^{51} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

R^{52} and R^{53} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{52} and R^{53} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

r is 0 to 4;

s is 0 to 4;

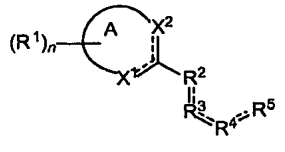
m is 0 to 4; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

36. The compound of claim 35 wherein X^1 is N.

37. The compound of claim 36 wherein X^2 is N.

38. A method of inhibiting $P210^{BCR\text{-}ABL\text{-}T315I}$ theramutein comprising administering to a human a compound having the formula I



(I)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^2 is selected from $-CR^{21}{}_a$-, $-NR^{22}{}_b$-, and $-(C=R^{23})$-;

each R^{21} is independently selected from H, halo, $-NH_2$, $-N(H)(C_{1\text{-}3}$ alkyl), $-N(C_{1\text{-}3}$ alkyl$)_2$, $-O-(C_{1\text{-}3}$ alkyl), OH and $C_{1\text{-}3}$ alkyl;

each R^{22} is independently selected from H and $C_{1\text{-}3}$ alkyl;

R^{23} is selected from O, S, N-R^0, and N-OR^0;

R^3 is selected from $-CR^{31}{}_c$- , $-NR^{32}{}_d$-, and $-(C=R^{33})$-;

each R^{31} group is selected from H, halo, $-NH_2$, $-N(H)(R^0)$, $-N(R^0)_2$, $-O-R^0$, OH and $C_{1\text{-}3}$

alkyl;

each R^{32} group is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, aryl, and a heterocyclic ring;

R^{33} is selected from O, S, N-R^{34}, and N-OR^0;

R^{34} is selected from H, NO_2, CN, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl and a heterocyclic ring;

R^4 is selected from $-CR^{41}_e$-, -NR^{42}_f-, -($C=R^{43}$)-, and -O-;

each R^{41} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, CO_2R^0, $C(O)R^0$, aralkyl, aryl, and a heterocyclic ring;

each R^{42} group is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, aryl, and a heterocyclic ring;

each R^{43} is selected from O, S, N-R^0, and N-OR^0;

with the provisos that when R^2 is $-NR^{22}_b$- and R^4 is $-NR^{42}_f$-, then R^3 is not $-NR^{32}_d$-; and that both R^3 and R^4 are not simultaneously selected from -($C=R^{33}$)- and -($C=R^{43}$)-, respectively;

R^5 is selected from -Y-R^6 and -Z-R^7;

Y is selected from a chemical bond, O, NR^0,

R^6 is selected from alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

Z is a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

R^7 is H or is selected from aryl and a heterocyclic ring;

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring;

a is 1 or 2;

b is 0 or 1;

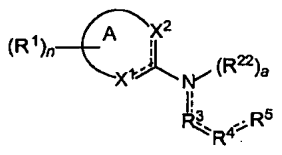
c is 1 or 2;

d is 0 or 1;

e is 1 or 2; and

f is 0 or 1.

39. The method of claim 38 comprising administering a compound having the formula I_a



(I_a)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

each R^{22} is independently selected from H and C_{1-3} alkyl;

R^3 is selected from $-CR^{31}{}_c-$, $-NR^{32}{}_d-$, and $-(C=R^{33})-$;

each R^{31} group is selected from H, halo, $-NH_2$, $-N(H)(R^0)$, $-N(R^0)_2$, $-O-R^0$, OH and C_{1-3} alkyl;

each R^{32} group is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, aryl, and a heterocyclic ring;

R^{33} is selected from O, S, N-R^{34}, and N-OR^0;

R^{34} is selected from H, NO_2, CN, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl and a heterocyclic ring;

R^4 is selected from $-CR^{41}_{e}$-, $-NR^{42}_{f}$-, -(C=R^{43})-, and -O-;

each R^{41} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, CO_2R^0, $C(O)R^0$, aralkyl, aryl, and a heterocyclic ring;

each R^{42} group is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, aryl, and a heterocyclic ring;

each R^{43} is selected from O, S, N-R^0, and N-OR^0;

with the provisos that when R^4 is $-NR^{42}_{f}$, then R^3 is not $-NR^{32}_{d}$-; and that both R^3 and R^4 are not simultaneously selected from -(C=R^{33})- and -(C=R^{43})-, respectively;

R^5 is selected from -Y-R^6 and -Z-R^7;

Y is selected from a chemical bond, O, N-R^0,

R^6 is selected from alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

Z is a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

R^7 is H or is selected from aryl and a heterocyclic ring;

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring;

a is 1 or 2;

b is 0 or 1;

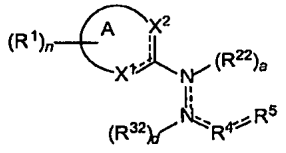
c is 1 or 2;

d is 0 or 1;

e is 1 or 2; and

f is 0 or 1.

40. The method of claim 38 comprising administering a compound having the formula I_b



(I_b)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

each R^{22} is independently selected from H and C_{1-3} alkyl;

each R^{32} group is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, aryl, and a heterocyclic ring;

R^4 is selected from $-CR^{41}{}_e$-, $-(C=R^{43})$-, and -O-;

each R^{41} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, CO_2R^0, $C(O)R^0$, aralkyl, aryl, and a heterocyclic ring;

each R^{43} is selected from O, S, N-R^0, and N-OR^0;

R^5 is selected from -Y-R^6 and -Z-R^7;

Y is selected from a chemical bond, O, N-R^0,

R^6 is selected from alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

Z is a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

R^7 is H or is selected from aryl and a heterocyclic ring;

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic

ring;

a is 1 or 2;

b is 0 or 1;

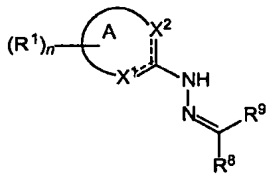
c is 1 or 2;

d is 0 or 1;

e is 1 or 2; and

f is 0 or 1.

41. The method of claim 38 comprising administering a compound having the formula II



(II)

wherein

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^8 is selected from the group consisting of is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, CO_2R^0, $C(O)R^0$, aralkyl, aryl, and a heterocyclic ring;

R^9 is selected from -Y-R^6 and -Z-R^7;

Y is selected from a chemical bond, O, N-R^0,

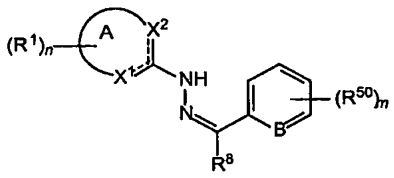
R^6 is selected from alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

Z is a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

R^7 is H or is selected from aryl and a heterocyclic ring; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

42. The method of claim 38 comprising administering a compound having the formula II_a



(II_a)

wherein

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^8 is selected from the group consisting of is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, CO_2R^0, $C(O)R^0$, aralkyl, aryl, and a heterocyclic ring;

X^3 is N, CH or C-R^{50};

each R^{50} is independently selected from the group consisting of alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{51}, $-(CH_2)_rC(O)(CH_2)_sR^{51}$, $-(CH_2)_rC(O)N(R^{52})(R^{53})$, $-(CH_2)_rC(O)O(CH_2)_sR^{51}$, $-(CH_2)_rN(R^{51})C(O)R^{51}$, $-(CH_2)_rN(R^{52})(R^{53})$, $-N(R^{51})SO_2R^{51}$, $-OC(O)N(R^{52})(R^{53})$, $-SO_2N(R^{52})(R^{53})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^{50} groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

R^{51} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

R^{52} and R^{53} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{52} and R^{53} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

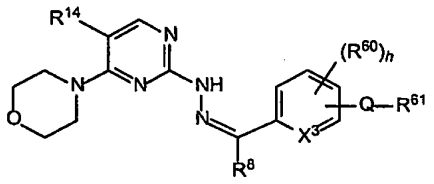
r is 0 to 4;

s is 0 to 4;

m is 0 to 4; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

43. The method of claim 38 comprising administering a compound having the formula II_b



wherein:

R^{14} is selected from H and F;

R^8 is selected from the group consisting of is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, CO_2R^0, $C(O)R^0$, aralkyl, aryl, and a heterocyclic ring;

X^3 is N, CH or C-R^{60};

each R^{60} is independently selected from the group consisting of alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^0, halo, aryl, and a heterocyclic ring;

R^{61} is selected from aryl and a heterocyclic ring;

Q is selected from a chemical bond or a group having the formula -O-, $-(CH_2)_i-$, $-(CH_2)_iC(O)(CH_2)_j-$, $-(CH_2)_i-N(R^{62})-(CH_2)_j-$, $-(CH_2)_iC(O)-N(R^{62})-(CH_2)_j-$, $-(CH_2)_iC(O)O(CH_2)_j-$, $-(CH_2)_iN(R^{62})C(O)-(CH_2)_j-$, $-(CH_2)_iOC(O)N(R^{62})-(CH_2)_j-$, and $-O-(CH_2)_i-C(O)N(R^{62})-(CH_2)_j-$;

R^{62} is selected from aryl, and a heterocyclic ring;

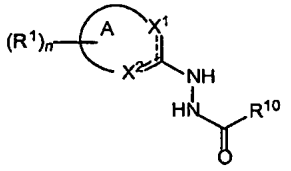
each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring;

h is 0 to 4;

i is 0 to 4; and

j is 0 to 4.

44. The method of claim 38 comprising administering a compound having the formula III



(III)

wherein

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused

ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

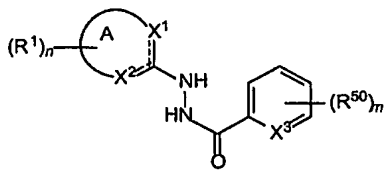
R^{10} is selected from -Y'-R^{18};

Y' is selected from a chemical bond, O, NR^0-, and a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

R^{18} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CF_3, aryl, and a heterocyclic ring; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

45. The method of claim 38 comprising administering a compound having the formula III_a



(III_a)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$,

$-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

X^3 is N, CH or C-R^{50};

each R^{50} is independently selected from the group consisting of alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{51}, $-(CH_2)_rC(O)(CH_2)_sR^{51}$, $-(CH_2)_rC(O)N(R^{52})(R^{53})$, $-(CH_2)_rC(O)O(CH_2)_sR^{51}$, $-(CH_2)_rN(R^{51})C(O)R^{51}$, $-(CH_2)_rN(R^{52})(R^{53})$, $-N(R^{51})SO_2R^{51}$, $-OC(O)N(R^{52})(R^{53})$, $-SO_2N(R^{52})(R^{53})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^{50} groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

R^{51} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

R^{52} and R^{53} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{52} and R^{53} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

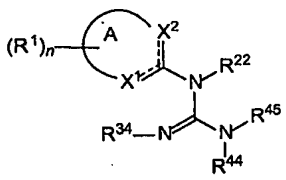
r is 0 to 4;

s is 0 to 4;

m is 0 to 4; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

46. The method of claim 38 comprising administering a compound having the formula IV



(IV)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^{22} is selected from H and C_{1-3} alkyl;

R^{34} is selected from H, NO_2, CN, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl and a heterocyclic ring;

R^{44} is selected from H, alkyl, cycloalkyl, $-(C=O)R^0$, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

R^{45} is selected from $-Y''-R^{19}$;

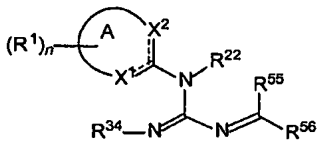
Y" is selected from a chemical bond, O, NR^0-, and a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl,

alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

R^{19} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CF_3, aryl, and a heterocyclic ring; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

47. The method of claim 38 comprising administering a compound having the formula V



(V)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^{22} is selected from H and C_{1-3} alkyl;

R^{34} is selected from H, NO_2, CN, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl and a heterocyclic ring;

R^{55} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

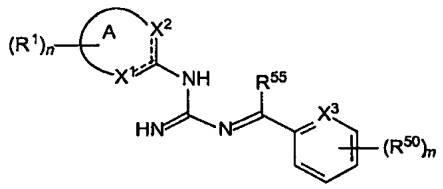
R^{56} is selected from -Y"-R^{19};

Y" is selected from a chemical bond, O, NR^0-, and a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

R^{19} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CF_3, aryl, and a heterocyclic ring; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

48. The method of claim 38 comprising administering a compound having the formula V_a



(V_a)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^{55} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

X^3 is N or C-R^{50};

each R^{50} is independently selected from the group consisting of alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{51}, $-(CH_2)_rC(O)(CH_2)_sR^{51}$, $-(CH_2)_rC(O)N(R^{52})(R^{53})$, $-(CH_2)_rC(O)O(CH_2)_sR^{51}$, $-(CH_2)_rN(R^{51})C(O)R^{51}$, $-(CH_2)_rN(R^{52})(R^{53})$, $-N(R^{51})SO_2R^{51}$, $-OC(O)N(R^{52})(R^{53})$, $-SO_2N(R^{52})(R^{53})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^{50} groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

R^{51} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

R^{52} and R^{53} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{52} and R^{53} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

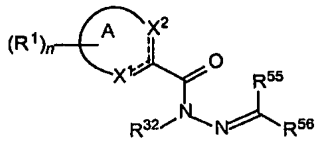
r is 0 to 4;

s is 0 to 4;

m is 0 to 4; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

49. The method of claim 38 comprising administering a compound having the formula VI



(VI)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^{55} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

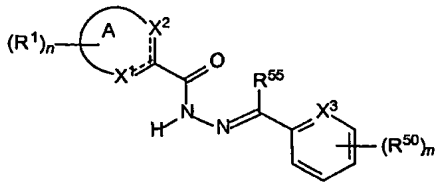
R^{56} is selected from -Y"-R^{19};

Y" is selected from a chemical bond, O, NR^0-, and a hydrocarbon chain having from 1 to 4 carbon atoms, and optionally substituted with one or more of halo, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CO_2R^0, $C(O)R^0$, $C(O)N(R^0)_2$, CN, CF_3, $N(R^0)_2$, NO_2, and OR^0;

R^{19} is selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CF_3, aryl, and a heterocyclic ring; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

50. The method of claim 38 comprising administering a compound having the formula VI_a



(VI_a)

wherein:

ring A is a 5-, 6-, or 7- membered ring or a 7- to 12-membered fused bicyclic ring;

X^1 is selected from N, N-R^0 or C-R^1;

X^2 is selected from N, N-R^0 or C-R^1;

the dotted lines represent optional double bonds;

each R^1 is independently selected from the group consisting of H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{11}, $-(CH_2)_pC(O)(CH_2)_qR^{11}$, $-(CH_2)_pC(O)N(R^{12})(R^{13})$, $-(CH_2)_pC(O)O(CH_2)_qR^{11}$, $-(CH_2)_pN(R^{11})C(O)R^{11}$, $-(CH_2)_pN(R^{12})(R^{13})$, $-N(R^{11})SO_2R^{11}$, $-OC(O)N(R^{12})(R^{13})$, $-SO_2N(R^{12})(R^{13})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^1 groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

n is 0 to 6,

each R^{11} is independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

each R^{12} and R^{13} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{12} and R^{13} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

p is 0 to 4;

q is 0 to 4;

R^{55} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

X^3 is N or C-R^{50};

each R^{50} is independently selected from the group consisting of alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^{51}, $-(CH_2)_rC(O)(CH_2)_sR^{51}$, $-(CH_2)_rC(O)N(R^{52})(R^{53})$, $-(CH_2)_rC(O)O(CH_2)_sR^{51}$, $-(CH_2)_rN(R^{51})C(O)R^{51}$, $-(CH_2)_rN(R^{52})(R^{53})$, $-N(R^{51})SO_2R^{51}$,

$-OC(O)N(R^{52})(R^{53})$, $-SO_2N(R^{52})(R^{53})$, halo, aryl, and a heterocyclic ring, and additionally or alternatively, two R^{50} groups on adjacent ring atoms form a 5- or 6-membered fused ring which contains from 0 to 3 heteroatoms;

R^{51} is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring;

R^{52} and R^{53} are independently selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, and a heterocyclic ring; or R^{52} and R^{53} may be taken together with the nitrogen to which they are attached form a 5- to 7- membered ring which may optionally contain a further heteroatom;

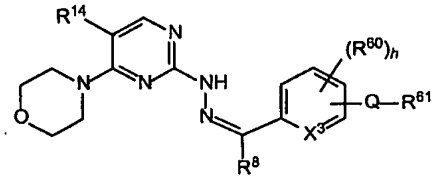
r is 0 to 4;

s is 0 to 4;

m is 0 to 4; and

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring.

51. The compound having the formula II_b



wherein:

R^{14} is selected from H and F;

R^8 is selected from the group consisting of is selected from H, alkyl, cycloalkyl, alkenyl, alkynyl, CO_2R^0, $C(O)R^0$, aralkyl, aryl, and a heterocyclic ring;

X^3 is N, CH or C-R^{60};

each R^{60} is independently selected from the group consisting of alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, CN, CF_3, NO_2, OR^0, halo, aryl, and a heterocyclic ring;

R^{61} is selected from aryl and a heterocyclic ring;

Q is selected from a chemical bond or a group having the formula -O-, $-(CH_2)_i-$, $-(CH_2)_iC(O)(CH_2)_j-$, $-(CH_2)_i-N(R^{62})-(CH_2)_j-$, $-(CH_2)_iC(O)-N(R^{62})-(CH_2)_j-$, $-(CH_2)_iC(O)O(CH_2)_j-$, $-(CH_2)_iN(R^{62})C(O)-(CH_2)_j-$, $-(CH_2)_iOC(O)N(R^{62})-(CH_2)_j-$, and $-O-(CH_2)_i-C(O)N(R^{62})-(CH_2)_j-$;

R^{62} is selected from aryl, and a heterocyclic ring;

each R^0 is independently selected from H, alkyl, cycloalkyl, aralkyl, aryl and a heterocyclic ring;

h is 0 to 4;

i is 0 to 4; and

j is 0 to 4.

52. A method for determining whether a substance is an inhibitor or an activator of a theramutein which capable of eliciting a detectable phenoresponse, which comprises:

a) incubating a first cell which expresses the theramutein at a substantially constant level with the substance;

b) incubating a second cell which expresses a corresponding prototheramutein at a substantially constant level with a known inhibitor or activator of the prototheramutein;

c) comparing a phenoresponse of the second cell to the known inhibitor or activator of the prototheramutein to the phenoresponse of the first cell to the substance; and

d) determining that the phenoresponse of the first cell is inhibited or activated to at least the same degree as the phenoresponse of the second cell is inhibited or activated by the known inhibitor or activator of the prototheramutein, thereby identifying the substance as an inhibitor or an activator of the theramutein.

53. The method of Claim 51, wherein the phenoresponse of the theramutein to the substance is greater than the phenoresponse of the prototheramutein to the known inhibitor or activator of the theramutein.

54. A method for determining whether a substance is a specific inhibitor or specific activator of a theramutein, which comprises:

a) providing a test cell which expresses the theramutein and which gives rise to a detectable phenoresponse;

b) treating the test cell with the substance;

c) examining the treated cell to determine whether the phenoresponse is modulated by treatment with the substance.

55. The method of Claim 1 or 2, wherein the theramutein or prototheramutein is a component of a signal transduction cascade.

56. The method of Claim 1 or 2, wherein the theramutein or prototheramutein is an enzyme.

57. The method of Claim 1 or 2, wherein the theramutein or prototheramutein is a protein kinase.

58. The method of Claim 1 or 2, wherein the theramutein or prototheramutein is a tyrosine kinase.

59. The method of Claim 1 or 2, wherein the theramutein or prototheramutein is a receptor tyrosine kinase.

60. The method of Claim 1 or 2, wherein the or prototheramutein is $p210^{Bcr\text{-}Abl}$.

61. The method of Claim 1 or 2, wherein the or prototheramutein is the T315I mutant of $p210^{Bcr\text{-}Abl}$.

62. The method of Claim 1 or 2, wherein the phenoresponse is a change in a cultural, morphological, or transient characteristic of the cell.

63. The method of Claim 1 or 2, wherein the phenoresponse includes phosphorylation of an intracellular substrate of the theramutein.

64. The method of Claim 1 or 2, wherein the phenoresponse is detected on a subcellular fraction of the cell.